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EXAMINER
AUDET, MAURY A

ART UNIT	PAPER NUMBER
1654	3

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/973,263	DEVORE ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- Th MAILING DATE of this communication app ars on the cov r sh t with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

1 The Information Disclosure Statement filed March 12, 2002 has been considered. An initialed copy of Form PTO-1449 in accordance with MPEP § 609 is attached.

Status of the Claims

2. Claims 1-20 are pending and examined on the merits.

Rejections

35 U.S.C. § 112, 2nd ¶ Indefinite

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. In claims 1 and 11, it is unclear what is contemplated within the meaning of "functional group"; wherein the first adhesive making step comprises "derivatizing collagen with a functional group" (see also § 112 Scope of Enablement Rejection below). The structure of a typical collagen molecule contains a triple helix, generally yielding more than a total of 3,000 amino acids, wherein all but glycine may have functional groups attached (See Alberts et al., Fig.19-40, p. 979). Since glycine is prevalent in the collagen molecule, it is indefinite as to where the functional groups of the derivatized collagen are capable of being attached? Claims 2 and 3 recite specific functional groups; however, no indication of what amino acids they are to

be attached, is indicated. It was not found in the specification where the functional groups in question were to be attached within the collagen molecule.

b. In claim 5, it is unclear whether claim 5 is meant to be depending from claim 1, 4, or 14 (or otherwise)? As it is improper for a preceding claim to depend from a succeeding claim, it is assumed that Applicant is not intending to depend from claim 14. If such is the case, it is nevertheless unclear whether claim 5 is to depend from claim 1 or 4 (or both as a MDC)? In order to analyze the breadth of the claims, amendment is necessary.

c. In claims 6 and 16, it is unclear what is meant by the term "adjust"? A description of the term "adjust" in connection with "concentration" was not found in the specification (i.e. a range associated therewith). [Note: The term "adjust" was only found in connection with pH (page 11, ¶2)]. Thus, it is unclear what the range of "adust[ment]" to the "concentration" is in claims 6 and 16? Applicant may point out where in the specification a description of the term "adjust" can be found, or amend claims 1 and 11 (see below, as suggested in §112 Scope of Enablement rejection for "concentration"), to distinctly claim the following or similar recitation: "adjust said concentration of said derivatized collagen from 300 mg/ml to 800 mg/ml in said composition"; to which claims 6 and 16 would necessarily contain proper antecedent basis then.

d. In claim 11, under the second proposed step, it is unclear what step has been taken, since the recitation of "increasing" is merely a result. Claim 11 is drawn, in part, to "increasing a concentration of said derivatized collagen in a composition." As opposed to claim 1, wherein the active step of "heating" was employed, in the second step, for increasing the concentration of derivatized collagen, no active 'step' has been claimed in claim 11. Specification page 10 describes "increasing" the concentration of derivatized collagen via thermal/heating methods:

"thermal energy . . . microwave energy . . . [o]ther heating methods can be employed such as direct application of a heat source." However, as claimed, it is unclear if "increasing" the concentration of derivatized collagen is carried out by the step of affecting the collagen itself (i.e. heating), or the other molecules in the composition (i.e. removal of water content or other molecules), or some other method? An 'active step' must be distinctly claimed which is employed for "increasing a concentration of derivatized collagen in composition".

35 U.S.C. § 112, 1st ¶ Scope of Enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

a. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a tissue "adhesive", does not reasonably provide enablement for *any and all* adhesives. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Specification page 1 (and throughout the entire specification) reasonably describes "[t]issue joining and sealing" compositions, patches, and methods of making such "tissue adhesives". However, the claims encompass a method of making an "adhesive", the latter language encompassing any and all adhesives (i.e. wood or metal (construction), pavement (transportation)). Applicant has not enabled such a broad scope.

Based on the highly unpredictable and complex nature of determining adhesive compatibility and capabilities (see ASI, 2000, Figures 2 (Chemical Type, Adhesives, Sealants)

and 3 (End Use, Adhesives, Sealants) teaching broad range of adhesives and sealants, and their fields of use), it cannot be determined whether Applicant's method of making an "adhesive" would work in making any other "adhesive" than a "tissue adhesive". Determining whether the method of making an adhesive, for any other purpose other than a tissue adhesive and whether that adhesive would have long-term viability, would require undue experimentation without a reasonable expectation of success by one of skill in the art.

Applicant may overcome the rejection by amending the claims to incorporate "tissue" before adhesive in the preamble (i.e. the type of "adhesive" described by the specification).

b. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for derivatizing collagen with sulfonyl/thiol (SH-) and carboxyl (COO-) "functional groups", does not reasonably provide enablement for derivatizing collagen with any and all "functional groups" (claim 1). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Specification page 9 (and generally throughout the specification) reasonably describes that "[d]erivatization was intended to provide functional groups to enhance both cohesive (SH-, thiol) and adhesive (COO-) characteristics", and that these specific "functional groups" were selected for their respective derivatizing qualities (i.e. SH- for cohesive strength; COO- for adhesive strength). However, the specification does not describe that any other functional groups could replace the two described "functional groups" (SH-; COO-) and produce a derivatized collagen capable of the cohesive and adhesive strength necessary to make the invention work. Applicant has not enabled such a broad scope.

Ellis et al. (1999) list 41 organic functional groups (Table 1) which are capable of reacting with proteins such as collagen, under the right conditions. As broadly claimed, the present invention as claimed, encompasses any one of Ellis et al.'s 41 organic functional groups. However, it is unpredictable whether even one of these could replace the "functional groups" described in the present specification. Furthermore, as Wallace et al. teach at column 31, lines 1-9, it took more than 100 hours of hydration in the study of simulated in vivo analysis of derivatized collagen to postulate that "weakening of bond strength was *thought* to be due to hydrolysis of carboxyl -ester and thio-ester (FIG. 13) network linkages. COH102 is a glutaryl-succinimidyl ester; even after reaction with the terminal carboxyl of the succinimidyl ester, there remains a carboxyl ester linking the glutaryl moiety to the main PEG chain; this bond, as well as the thio-ester bond, could hydrolyze" (emphasis added in original). Assuming it may only be possible to determine "functional group" bond strength by similar tests, the amount of time and effort to determine whether other "functional groups" could work in the invention would involve undue experimentation. Thus, determining whether any and all functional groups could elicit tissue cohesion and adhesion qualities, the two qualities described in the specification as essential to the invention's functionality, would require undue experimentation without a reasonable expectation of success by one of skill in the art.

Applicant may overcome the rejection by amending claim 1 to incorporate "with SH- and COO- functional groups" (i.e. the "functional groups" described by the specification).

c. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a "concentration" [of derivatized collagen] ranging from 300 mg/ml (30%) to 800 mg/ml, does not reasonably provide enablement for a "increase[ing] a

concentration" (claims 1 and 11) range below or above this concentration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Specification page 3, ¶ 2, reasonably describes that the "compositions are comprised of chemically derivatized soluble collagen, which is formulated to *concentrations* ranging from 300 mg/ml (30%) to 800 mg/ml (80%) collagen protein" (emphasis added in original). Further, on the middle of page 10, the specification describes that "[l]yophilized derivatized collagens were formulated into viscous compositions having from 30-80% collagen solids. Since collagen typically becomes saturated at less than 10% solids, *novel techniques were developed* to increase total collagen concentrations to 30-80%" (emphasis added in original). Based on the specification description, it can only be assumed that derivatized collagens containing "less than 10% solids" were being used in the art at the time of the invention, and that Applicant specifically found a novel technique to raise this percentage and that the percentage 300mg/ml (30%) to 800 mg/ml (80%) was found to be essential to the invention's functionality. Were this not the case, the only reasonable assumption is the specification would have described a functional concentration of any percentage around 100 mg/ml (10%) (i.e. just above the known solid concentration) to 800 mg/ml (80%) collagen solids. Applicants have not enabled such a broad scope of any "concentration".

As discussed above, Wallace et al. teach, at column 31, lines 1-9, that it took more than 100 hours of hydration in the study of simulated *in vivo* analysis of derivatized collagen to postulate that certain bonds may be weakened more readily than others. Likewise, it could take even more hours to test the specific collagen percentages necessary to work properly as a "tissue

adhesive". As broadly claimed, it is necessarily unpredictable as to whether any amount other than 30-80% would allow adequate long-term tissue adhesion in the present invention. Thus, determining whether a collagen solid concentration above or below 300 mg/ml (30%) to 800 mg/ml (80%) could elicit the necessary tissue cohesion and adhesion qualities, would require undue experimentation without a reasonable expectation of success by one of skill in the art.

Applicant may overcome the rejection by amending claims 1 and 11 to incorporate the following or similar recitation: "a concentration of said derivatized collagen consisting of 300 mg/ml (30%) to 800 mg/ml (80%) in said composition" (i.e. the "concentration" described by the specification).

d. Claims 7-9 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pH range between 6.8 – 7.8 (claims 7 and 17, and specification page 11), does not reasonably provide enablement for any and all pH ranges. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Specification page 11 describes that "[i]n both cases, it was critical to adjust the gelatinized collagen pH to 6.8-7.8 prior to preparing solder films." "These collagen-based solders appeared to provide the best biomechanical and adhesive characteristics." This range being critical, no other description of any other ranges was found in the specification. Applicants have not enabled the broad scope of any "desired range".

As discussed above, Wallace et al. teach, at column 31, lines 1-9, that it took more than 100 hours of hydration in the study of simulated *in vivo* analysis of derivatized collagen, to postulate that certain bonds may be weakened more readily than others. Likewise, it could take

even more hours to test the specific pH ranges of the derivatized collagen necessary to work properly as a tissue adhesive. As broadly claimed, it is necessarily unpredictable as to whether any pH other than a pH of 6.8-7.8 would allow the making of a derivative collagen composition capable of adequate long-term tissue adhesion as described in the present invention. Thus, determining such whether a collagen with a pH above or below 6.8-7.8 was capable of the necessary cohesive and adhesive qualities, would require undue experimentation without a reasonable expectation of success by one of skill in the art.

Applicant may overcome the rejection by amending claims 7 and 17 to incorporate the following or similar recitation: "adjust a pH of said composition to be within 6.8-7.8." [i.e. incorporating dependent claims 8 and 18 respectively into claims 7 and 17 and the pH described in the specification).

e. In response to the four 112 1st scope of enablement rejections, Applicant is asked to claim in full, clear, concise and exact terms, the elements of the invention as to enable *any* person skilled in the art to make and use the invention as claimed.

35 U.S.C. § 102: Anticipation

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

a. Claims 1-3, and 5-20 are rejected under § 102, as anticipated by Kelman et al. (US 5,219,895).

The claimed invention (cl. 1-10) is drawn to a "a method of making an adhesive, comprising the steps of: derivatizing collagen (extracting from a tissue source (cl. 2); an animal tissue (cl. 3)) with a functional group (reacting said collagen with 4-mercapto-1,8-naphthalic anhydride (cl. 4); with glutaric anhydride (cl. 5)); and heating (additional heating steps to adjust said concentration (cl. 6)) a composition including said derivatized collagen to thereby increase a concentration of said derivatized collagen in said composition. The claimed invention is further drawn to a step of adding a pH altering material (NaOH (cl. 9)) to said derivatized collagen to thereby adjust a pH of said composition within a desired range (6.8-7.8 (cl. 8)). The claimed invention (cl. 11-20) is also more broadly drawn to a "increasing concentration of said derivatized collagen in a composition (comprising a plurality of heating steps to adjust said concentration of said derivatized collagen (cl. 17))".

Kelman et al. (also cited in Paper No. 2, Applicant's IDS) teach Applicant's claims 1-3, 5-9, 11-13, and 15-20, by teaching a method of making (cl. 17) an adhesive (title) comprising the steps of reacting collagen (cl. 17), defined as being derived (defined further as extracted (column 3, line 58)) from a human or animal tissue (claim 4), with at least one of a [functional groups] acylating agent and sulfonating agent [i.e. derivatizing/derivatized collagen with a functional group](cl. 17 (b)), wherein the acylating agent may be glutaric anhydride (cl. 24). Kelman et al. also teach more specifically in claim 17 (b) "reacting said partially fibrillar collagen with at least one of an acylating agent and sulfonating agent at a pH ranging from 7.5-10.0 and at a temperature ranging from 4 C to 37 C [i.e. heating a composition to increase derivatized collagen concentration in composition; increasing a concentration of derivatized collagen in composition]." Kelman et al. further defines the claim 17 (b) step of making the derivatized

collagen in part through temperature controls [i.e. heating] by teaching "[t]he extent of acylation [i.e. concentration of derivatized collagen in composition] may be modulated by varying . . . the temperature and the time of the reaction" [i.e. additional/plurality of heating steps over time to adjust the concentration of the derivatized collagen in concentration; because as defined the Kelman et al. teaching can be interpreted as heating at a varied temperature which could be conducted over a varied timeframe]. Kelman et al. further teach a pH from about 7.0 to 7.5 [i.e. within "desired range is 6.8-7.8"] by addition of sodium hydroxide solution [i.e. NaOH]." (column 5, lines 1, 6, 28-30 and 38-40).

b. Claims 1, 5-10, 11, and 15-20 are further rejected under § 102, as being anticipated by Wilkie et al. (US 2002/0022588 A1, Feb. 21, 2002).

The invention is discussed above.

Wilkie et al. teach derivatizing collagen (700 mg; 20-45%) with glutaric anhydride [COO- functional group] wherein the resulting solution [composition] is then titrated to a pH of 6.5-7.5 using NaOH (page 18, column 2, Example 5) and may also be heated [and additionally heated] to increase the viscosity [concentration] of derivatized collagen in composition (page 6, last sentence; example using albumin, but note claim 3 and taught throughout that either collagen or albumin may be used as the protein of the adhesive), and that collagen and fibrin [i.e. collagen fibers, fibrils] may be used for their bioadhesive or sealant properties of the cross-linked [derivatized collagen] (page 3, column 2, 2nd ¶).

c. Claims 1-3 are further rejected under § 102, as being anticipated by Devore et al. (US 6197934).

The invention is discussed above.

Devore et al. teach heating [and additional heating] a derivatized [COO-] collagen (column 1, lines 44-47), to a pH of 7.4 (column 4, line 31) and the use of NaOH as a pH altering material (column 4, line 22).

35 U.S.C. § 103 Obviousness

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

a. Claims 1-20 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Kelman et al. (US 5129895), in view of Devore et al. (US 6161544) and Wallace et al. (US 6495127).

The claimed invention is discussed above, including claim 4, drawn to reacting the derivatized collagen with 4-Mercapto-1,8,Naphthalic Anhydride.

Kelman et al. is discussed above. Kelman et al. teach the use of sulfonating agents (SH-), emphasizing the list as "non-limiting", with a derivatized collagen (column 4, line 47-65). Kelman et al. does not specifically teach the use of 4-Mercapto-1,8,Naphthalic Anhydride [Applicant's claim 4 and 14].

Devore et al. teach an orthokeratology procedure utilizing as one step of the procedure crosslinking agents and anhydrides for destabilizing/restabilizing a collagen matrix (column 3, lines 5-10), wherein a suitable, but non-limiting example of potential anhydrides include: 4-Mercapto-1,8,Naphthalic Anhydride [column 6, lines 49]. Like Kelman et al., Devore et al. listed many sulfonating agents, as suitable, but non-limiting examples, all capable of carrying out the same function: restabilizing collagen matrix by allowing crosslinking (i.e. for cohesive

strength. One of ordinary skill in the art would have found it prima facie obvious to use the 4-Mercapto-1,8,Naphthalic Anhydride of Devore et al. in the method of making a derivatized collagen composition of Kelman et al., because the express teaching by Devore et al. (like Kelman et al.) that the listed sulfonating agents are merely "non-limiting", without distinguishing 4-Mercapto-1,8,Napthalic Anhydride, defines the group much like Markush claim language where any one of the group are interchangeable/obvious variants to equate the desired result.

Kelman et al. teach "as further embodiments of the present invention, the sealant and adhesive formulations can be used as systems specific for delivery of numerous . . . biological compounds [i.e. material selected from the group of collagen fibrils, etc.]. Such materials can be added to the collagen adhesive or sealant to promote cell migration, cell adhesion, and wound healing [i.e. collagen fibers, etc.] (column 6, lines 64-68, and column 7, line 1). However, Kelman et al. does not specifically teach "adding a material selected from the group of collagen fibrils, collagen fibers and collagen fiber bundles" [Applicant's claims 10 and 20].

Wallace et al. teach a composition with derivatized collagen and optional composition constituents; "particularly preferred is collagen, which may be in the form of afibrillar, microfibrillar [i.e. fibrils] or fibrillar [i.e. fibers] collagen." (column 10, lines 45-46). Wallace et al. teach that collagen "may improve biocompatibility of the matrix, including the potential colonization by cells [i.e. cell migration], promotion of wound healing, etc." (column 10, lines 33-35) and ". . . structural integrity [i.e. cell adhesion] of the matrix by becoming crosslinked thereto along with the other matrix components" (column 10, lines 37-39). Wallace et al. teach the same three reasons for adding a species (collagen fibrils or fibers) of Kelman et al.'s genus ("biological materials"), to a tissue adhesive composition containing derivatized collagen (column

6, lines 64-68, and column 7, line 1): "cell migration, cell adhesion, and wound healing". One of ordinary skill in the art would have found it prima facie obvious to add the collagen fibrils or fibers of Wallace et al. to the derivative collagen composition of Kelman et al., because the addition of fibers would provide a greater degree of adhesive and cohesive strength to the sealant for promoting cell migration, cell adhesion, and wound healing; the desired outcomes of the sealant.

b. Claims 1-20 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Wilkie et al. (0022588 A), in view of Kelman et al. and further in view of Devore et al. (6161544).

The claimed invention is discussed above.

Wilkie et al. is discussed above.

Wilkie et al. teach the making of derivatized collagen in a composition, but does not teach attaining the collagen from a tissue source, namely animal tissue tissue [Applicant's claims 2-3 and 12-13].

Kelman et al. teach a method of making a "biologically compatible" (column 3, lines 38-39) derivatized collagen wherein the collagen is derived (defined further as extracted (column 3, line 58)) from a human or animal tissue (claim 4). One of ordinary skill in the art would have found it prima facie obvious to use collagen from a tissue source, and specifically an animal tissue in Wilkie et al., because Kelman et al. teach the need for biological compatibility when using the derivatized collagen as a sealant on animals (i.e. humans); and prevent rejection of the sealant as an antigenic source.

Wilkie et al. teach derivatizing collagen with a functional group (glutaric anhydride; COO-), but does not specifically teach the use of 4-Mercapto-1,8,Napthalic Anhydride

[Applicant's claims 4 and 14]. Kelman et al. teach the use of glutaric anhydride to derivatize collagen with the COO- (carboxyl) functional group and also with SH-. Kelman et al. teach that derivatizing (polymerizing) collagen with COO- and SH-, produces a composition with adhesive and sealant properties (column 2, lines 57-58). Kelman et al. teach the use of sulfonating agents (SH-), emphasizing the list as "non-limiting", with a derivatized collagen (column 4, line 47-65). Devore et al. does specifically teach the use of 4-Mercapto-1,8,Napthalic Anhydride (and the combination of Devore et al. and Kelman et al. are discussed in full above and applied equally here). One of ordinary skill in the art would have found it prima facie obvious to derivatize the collagen of Wilkie et al. with an SH- functional group because Kelman et al. teach it is capable of adhesive and sealant properties; and further with the 4-Mercapto-1,8,Napthalic Anhydride of Devore et al. in the method of making a derivatized collagen composition in view of Kelman et al., because the express teaching by Devore et al. (like Kelman et al.) that the listed sulfonating agents are merely "non-limiting", without distinguishing 4-Mercapto-1,8,Napthalic Anhydride, defines the group much like Markush claim language where any one of the group are interchangeable/ obvious variants to equate the desired result.

c. Claims 1-20 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Devore et al. (US 6197934), in view of Wilkie et al. and Wallace et al. and Kelman et al. and further in view of Devore et al. (6161544).

The claimed invention is discussed above.

Devore et al. (934)is discussed above.

Devore et al. (934) teach the making of derivatized collagen in a composition, but does not teach attaining the collagen from a tissue source, namely animal tissue tissue [Applicant's

claims 2-3 and 12-13]. The same argument for combination of Kelman et al. with Wilkie et al. (subsection §103 a. above) is equally applied with Devore et al.

Devore et al. teach derivatizing collagen with a functional group (glutaric anhydride; COO-), but does not specifically teach the use of 4-Mercapto-1,8,Napthalic Anhydride [Applicant's claims 4 and 14]. The same argument for combination of Kelman et al. further in view of Devore et al. (6161544) is equally applied with Devore et al.

Devore et al. teach the use of adhesive composition for collagen stabilization and wound closure (column 1, line 28-29) with derivatized collagen, but does not specifically teach also "adding a material selected from the group of collagen fibrils, collagen fibers and collagen fiber bundles" [Applicant's claims 10 and 20]. Wallace et al. teach a composition with derivatized collagen and optional composition constituents; "particularly preferred is collagen, which may be in the form of afibrillar, microfibrillar [i.e. fibrils] or fibrillar [i.e. fibers] collagen." (column 10, lines 45-46). Wallace et al. teach that collagen "may improve biocompatibility of the matrix, including the potential colonization by cells [i.e. cell migration], promotion of wound healing, etc." (column 10, lines 33-35) and ". . . structural integrity [i.e. cell adhesion] of the matrix by becoming crosslinked thereto along with the other matrix components" (column 10, lines 37-39). One of ordinary skill in the art would have found it prima facie obvious to add the collagen fibrils or fibers of Wallace et al. to the derivative collagen composition of Devore et al., because Wallace et al. teach that the addition of fibers would provide a greater degree of adhesive and cohesive strength to the sealant for promoting collagen stabilization and wound closure; desired outcomes of sealants.

Nonstatutory Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4, 17, and 24 of U.S. Patent No. 5,219,895 (Kelman et al.; common inventor Dale P. Devore) in view of Devore et al. and Wallace et al.

The teachings of Kelman et al. have been fully discussed under the §§ 102 and 103 rejections.

The teachings of Devore et al. and Wallace et al. have been fully discussed under the § 103 rejections.

The reasons for rejection of claims 1-20 have been fully addressed in the §§ 102 and 103 rejections and are maintained under the same grounds in the present Nonstatutory Double Patenting rejection.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 703-305-5039. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-1234 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

MA
April 27, 2003

MICHAEL MELLER
PRIMARY EXAMINER